MICROSTIMULATION OF LUMBOSACRAL SPINAL CORD-MAPPING

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Fifth Progress Report
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Neural Prosthesis Program

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This QPR is being sent to you before it has been reviewed by the staff of the Neural Prosthesis Program.

I. Introduction

In previous quarterly progress reports we have presented data which indicate that lower hindlimb (shank) flexion and extension, about the knee joint, could be produced by microstimulation of specific sites in the lumbo-sacral spinal cord. During those preliminary studies a number of potential problems that could effect the interpretation of our results were identified. These problems are listed below and addressed in this report:

(1) The rotational torque sensor used in these experiments measured net torque, so that both flexion and extension could occur simultaneously and only the net resulting torque would be measured. The degree of selectivity of our spinal cord map of stimulus sites would be somewhat unclear as to whether this was pure extension or a mixture of extension and flexion - with the extensors producing the greater torque. One solution that we used during this quarter was to record the electromyographic (EMG) activity from both knee joint flexors and extensors muscle groups. Although EMG activity does not provide a direct measure of torque generated for a particular muscle; it does provide an indication of activity in that particular muscle and the amplitude of the EMG indicates the intensity of activation.

(2) The hindlimb position at the time of spinal cord microstimulation may change the magnitude of the torque response. In all our previous experiments we maintained 120° angle between the femur and tibia at the knee joint. This was the approximate angle that the leg assumed in the anesthetized cat with no tension placed on the leg. During experiments this quarter we varied the angle formed at the knee joint by the femur and tibia from 60° (very near maximum flexion) to 150° (nearly maximal extension). The

results showed that changes in knee joint angle could effect peak torque but the magnitude of this change was small.

(3) A third problem that seems to be present with certain site of stimulation is the contraction of the hip flexors, extensors and abductors occurs and may alter the exact torque recorded about the knee joint. There is also small movement of the femur that could occur with knee joint movement. These are issues of both selectivity and; one of proper immobilization of the preparation. The selectivity issue can be controlled for by additional EMG recording from the hip muscles that produce hip flexion, extension and abduction. The complete immobilization of the femur requires the addition of hardware to pin the femur. We constructed this hardware during this quarter and experimented with various designs to produce complete immobilization with minimum damage to the muscles.

During this quarter we also continued our tracing studies with pseudorabies virus in the cat . These studies examine both neurons involved in extension about the knee joint and those involved in penile erection.

II. Rotational Torque and EMG Recordings During Extension of the Hindlimb to Microstimulation of the Lumbar Spinal Cord.

As mentioned in the introduction the hindlimb torque measured during microstimulation of the lumbar cord is a <u>net</u> torque. These studies used EMG recording form various muscle groups to determine which muscles were active during hindlimb extension. The methods used were similar to those described in previous progress reports and will be summarized below. Cats were anesthetized with halothane-oxygen followed by pentobarbital (25 - 30 mg/kg iv). Figure 1 shows the general experimental setup. A light-weight aluminum bar was attached to the tibia by two screws. The rotational torque sensor attaches to this bar by means of a set-screw, allowing the positioning of the knee joint at different angles. The output of the torque sensor is amplified, displayed on a chart recorder, recorded on tape, digitized, and stored in a computer for further analysis. The spinal cord is stimulated with fine tipped (300 - 400 μ^2 surface area) activated iridium electrodes at 200μ intervals along the electrode penetration. During our most recent experiments we have added eight EMG electrodes, four in the shank extensor muscles (quadriceps femoris) and four in the shank flexor muscles (biceps femoris and semitendinosus). The EMG activity was amplified, digitized at 2000 Hz, stored and displayed in a similar manner to the accompanying torque information.

Stimulus artifact in the EMG recording was reduced to a minimum by careful grounding and the use of bipolar recording. However, some artifact was always present but was small when compared to the amplitude of EMG (Figures 2, 3, and 4). In addition the stimulus artifact was of very short duration (0.2msec) while the evoked EMG had a duration of many milliseconds (25 - 50msec). The artifact could easily be distinguished from the EMG activity (Figure 4). A blanking circuit is also being constructed to further reduce the stimulus artifact in our EMG recordings.

Simultaneous recording of extensor and flexor torque and extensor and flexor EMG at two (40 and 80 Hz) different frequencies of stimulation are shown in Figures 2 and 3. The extensor EMG is large and follows the torque response quite closely, while the flexor EMG is flat. The spikes seen on the flexor EMG traces are stimulus artifact (Figures 2 and 3, bottom traces). Also seen in Figures 2 and 3 are the effects of two different frequencies of simulation - 40 and 80 Hz. During a sustained contraction, fatigue often occurs in skeletal muscle. The fatigue is seen as a reduction in torque amplitude and occurs at high frequencies of stimulation. Notice that in Figure 3 at 80 Hz stimulation the torque curve is initially high and then slowly drops. At 40 Hz simulation, seen in Figure 2, the reduction in torque over the duration of the muscle activation is small. The EMG activity at both 40 and 80 Hz reflect the changes in torque amplitude. When fatigue occurs at 80 Hz the amplitude of the EMG is also reduced in a similar manner. Changes in intensity of stimulation can also alter torque, this is likewise reflected in changes in EMG amplitude.

With L_6 ventral root stimulation or with non-selective microelectrode simulation both flexors and extensors are often activated. In this instance EMG activity is seen from both flexors and extensors but the net torque is seen in the direction of extension. The EMG usually reflects the increase activity of the extensor with a larger amplitude EMG from the extensor muscle groups. Furthermore, movement of the microelectrode tip from an active site to an inactive site produces a decrease in both torque amplitude and EMG activity. These results, taken together, suggest that the extensor torque generated by microstimulation of the spinal cord is due mainly to activation of extensor muscles while flexor muscles remain inactive. This data also suggests that EMG activity may be an appropriate indicator of muscle groups contributing to the torque response recorded. By using a larger number of EMG electrodes distributed over a greater muscle mass these results may be even more convincing.

These studies will continue into the next quarter, with EMG recording becoming a standard part of our mapping experiments.

III. The Effects of Changes in Knee Joint Angle on Extension and Flexion Torque.

All previous mapping experiments have been performed at a knee joint angle of 120° (see Figure 5). Since it is known that the amount of stretch or tension placed on striated muscle prior to its activation can change the amount of force generated, it seem important that this parameter be examined in a few experiments to determine if torque recorded in our experiments varied greatly over various angles of the hindlimb about the knee joint.

The experimental setup was the same as described above. Once the location of a site which produced a selective response to microstimulation of the lumbar cord was determined, a series of experiments were performed. Figure 5 shows the results from one experiment in which the L_5 spinal cord was stimulated with a microelectrode. This site produced a pure extensor torque response using EMG recording from both flexor and extensor muscle groups as an indication. The angle of the knee joint was systematically changed from an angle of 60° to 150° (Figure 5). The torque generated at each angle was recorded and each angle was studied several times and a mean torque calculated. The graph in Figure 5 shows the maximum mean torque (in this case extension) generated at four different angles from 150° (maximal extension) to 60° (maximal flexion). Notice that the difference in torque generated at each angle was small. The largest difference was seen at 150° where there was a small decrease in extensor torque. At 60, 90, and 120° of angle the responses were nearly identical, with 120° being only slightly larger than 60° and 90°.

From these preliminary studies with extensor torque it does not seem that knee joint angle is a significant factor in generating a map of the extensor responses to cord stimulation.

These studies will continue in the next quarter to determine if flexor torque is more or less susceptible to changes in knee joint angle.

IV. Immobilization of the Femur.

During this quarter we designed and constructed several types of hardware to immobilize the femur. The simple solution of a single pin through the femur does not appear adequate to prevent small movement of the femur about the hip joint, since the femur can rotate around a single pin. Changes in femur position although small seem to be transmitted to torque sensor and recorded as hindlimb torque (either flexor or extensor). Movement of the femur may also have the opposite effect of reducing the hindlimb torque generated by shank flexion or extension.

The best solution seemed to be a plate with two parallel screws into the femur. There however was some concern about the size of the hardware and the amount of surgery necessary to attach the plate. The plate and surgical procedure may actually damage or interfere with some of the extensor muscles.

We will test, during the next quarter, a smaller piece of hardware which seems to provide adequate support with little interference to important muscles of shank flexion and extension.

Figure 1 Schematic diagram showing the experimental setup. A bar is attached to the tibia of the cat's hindlimb by two screws. This bar supports a rotational torque sensor which measures the isometric torque produced at the shank (lower hindlimb) about the knee joint. The output of the torque sensor is amplified, displayed on the chart recorder, recorded on magnetic tape, digitized, and stored on the hard drive of the computer. A laminectomy exposed the surface of the spinal cord and a fine tipped activated iridium microelectrode is used for focal stimulation of the various sites in the spinal cord, at 200μ increments along a given penetration. The stimulus information (not shown) is also stored on the computer hard drive.

Figure 2 Computer generated plots showing changes in flexion and extension torque (top trace) and EMG from hindlimb extensor (middle trace) and flexor (bottom trace) muscles to microstimulation of the L_5 cord. Dotted lines on EMG plots represent the stimulus artifact level. Notice that the plot of flexor EMG is only stimulus artifact, while the plot for extensor EMG is stimulus artifact with large EMG response. The stimulus artifact for the extensor EMG plot is negative (downward deflection) while that for flexion is positive (upward deflection), see also Figure 4. Notice that the EMG correlated very well with the extension torque produced. No flexion torque or flexor EMG is generated at the site of stimulation. The stimulus frequency for this response is 40 Hz. Other stimulus parameters are: 100μA, 200μsec, 30 seconds on, 2 minutes off. Site of stimulation is 5.6mm from the surface in L_5.

Figure 3 Computer generated plots showing changes in flexion and extension torque and EMG. Same as figure 2 except that the frequency of stimulation is 80Hz. Notice with an 80Hz stimulus, fatigue (decreases in torque with time) occurs rapidly. The extensor EMG also decreases in amplitude reflecting the loss of torque. Compare this figure to figure 2. Other stimulus parameter and site the same as figure 2.

Figure 4 Computer generated plots showing changes in extensor (top plot) and flexor (bottom plot) EMG activity to microstimulation of the L_5 spinal cord. The same EMG data as shown in Figure 2 except at a faster time base. In the top plot of the extensor EMG arrows mark the negative-going stimulus artifact which had a duration of 200μsec. The remaining wave form is the EMG recorded from the quadriceps muscle. There is no flexor EMG activity only the stimulus artifact (bottom plot). The stimulus is at 40Hz (25msec interval between stimuli) and the duration is 200μsec. The data is digitized at 2000 samples/sec (one sample every 500μsec). Since the pulse duration is short (200μsec) some artifact pulses are missed or reduced in amplitude due to the sampling rate. The main point of this figure is to show that the stimulus artifact does not distort the EMG to any great extent.

Figure 5 A graph showing the change in maximal extension torque with changes in knee angle for four different angles: A=60°, B=90°, C=120°, and D=150°. The figurine in the upper right is the schematic of the cat hindlimb showing the different knee joint angles plotted in the graph. The knee angle is formed by the bones of the upper and lower leg (the tibia and femur) which join at the knee.

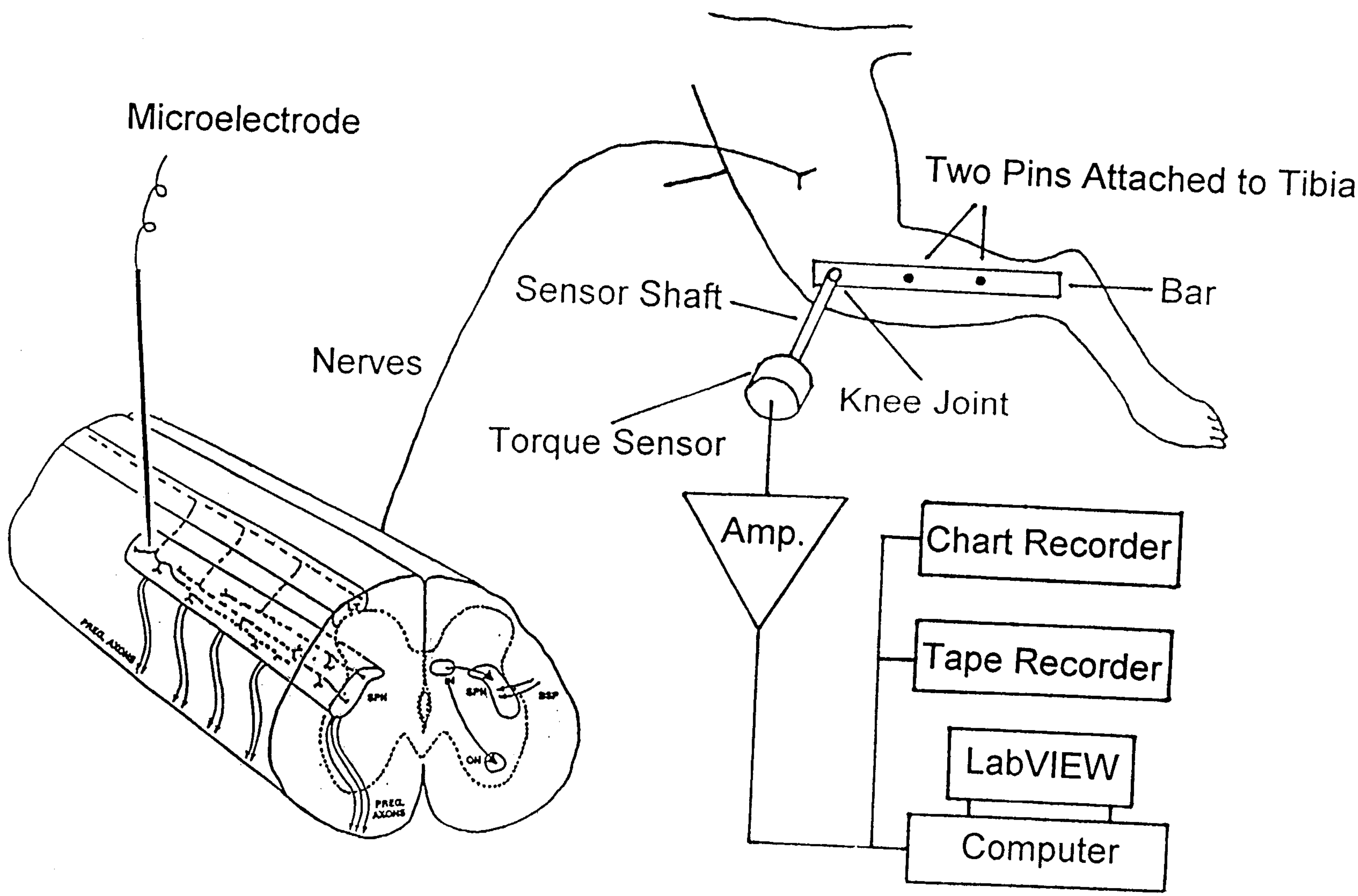
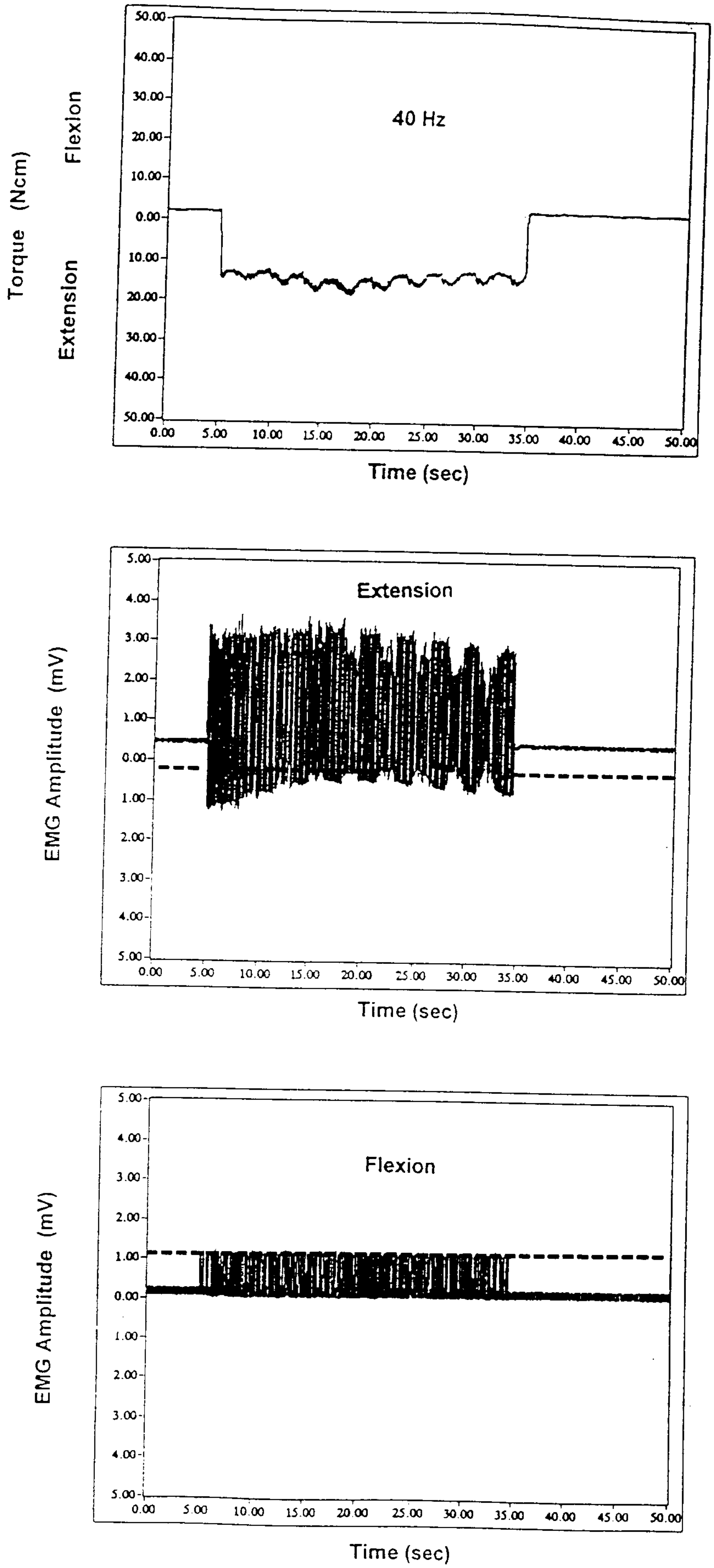
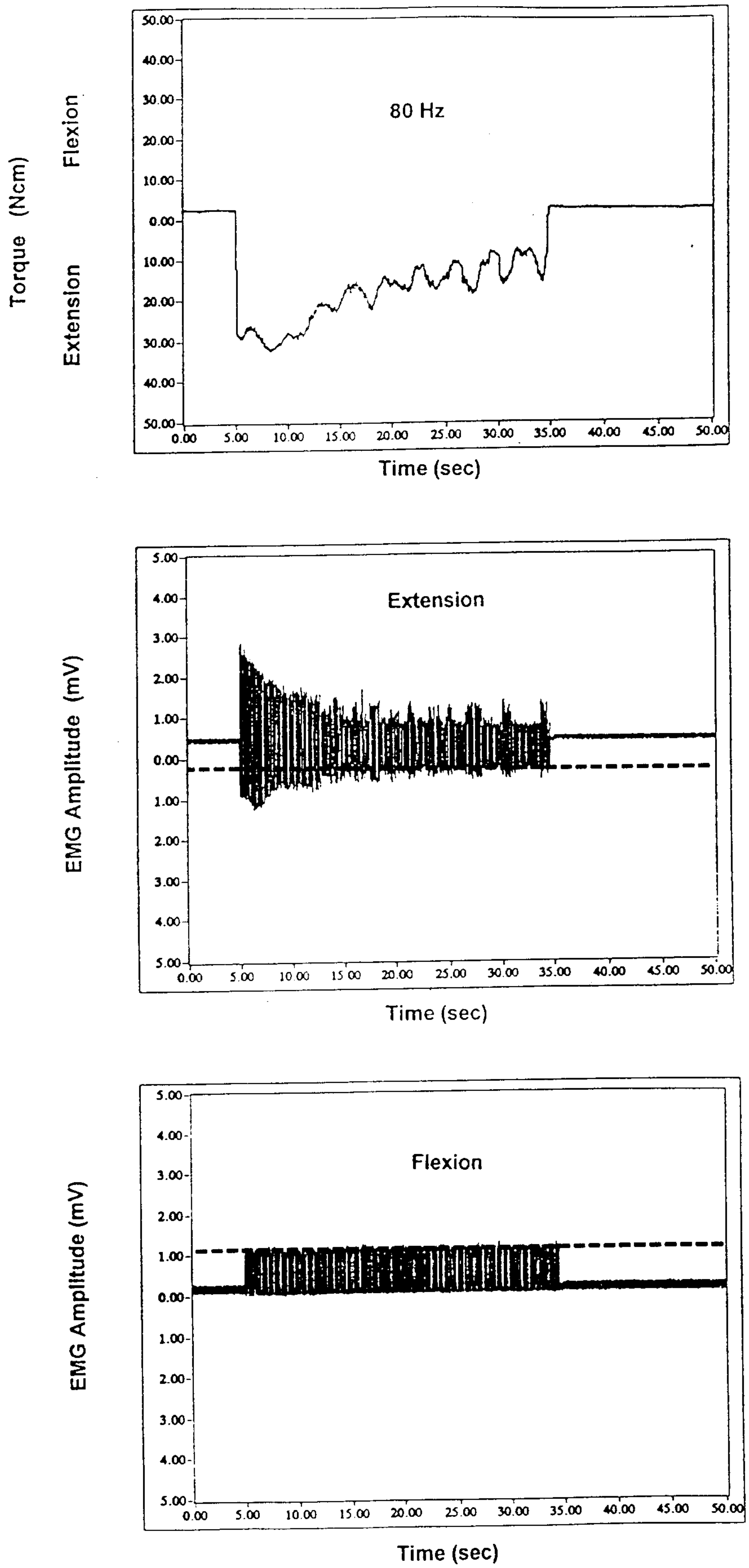

Microelectrode
Nerves
Sensor Shaft
Torque Sensor
Two Pins Attached to Tibia
Bar
Knee Joint
Amp.
Chart Recorder
Tape Recorder
LabVIEW
Computer

Figure 1



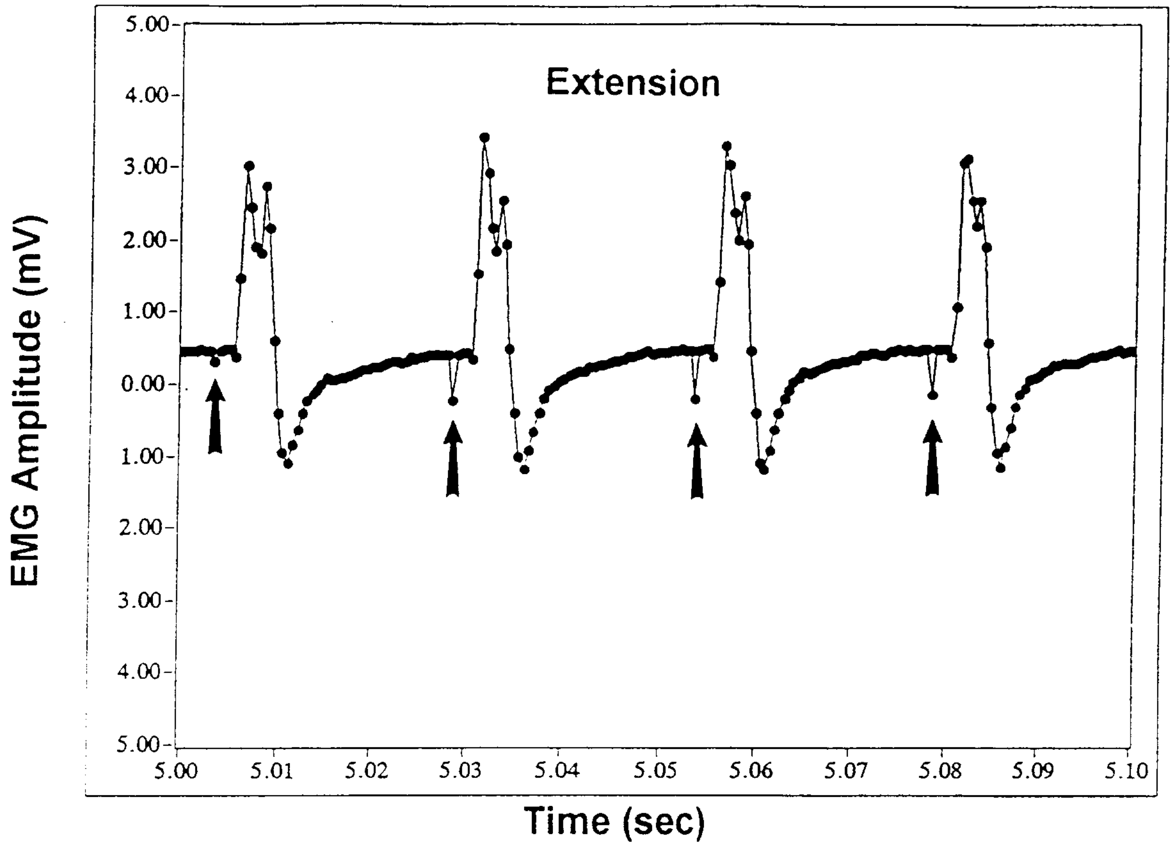
Torque (Ncm)
Flexion
Extension
40 Hz
Time (sec)
EMG Amplitude (mV)
Extension
Time (sec)
EMG Amplitude (mV)
Flexion
Time (sec)

Figure 2



80 Hz
Torque (Ncm)
Flexion
Extension
Time (sec)
Extension
EMG Amplitude (mV)
Time (sec)
Flexion
EMG Amplitude (mV)
Time (sec)

Figure 3


Extension
EMG Amplitude (mV)
Time (sec)
5.00
4.00
3.00
2.00
1.00
0.00
1.00
2.00
3.00
4.00
5.00
5.00 5.01 5.02 5.03 5.04 5.05 5.06 5.07 5.08 5.09 5.10

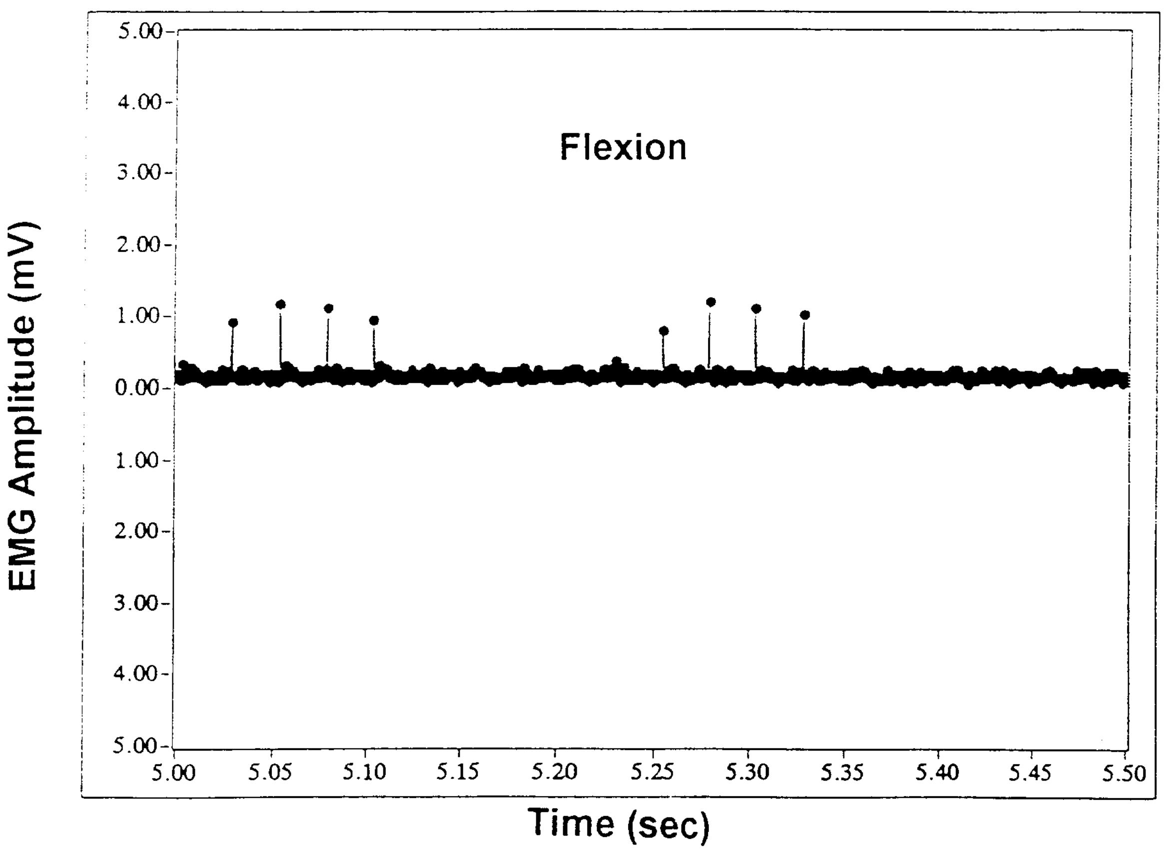
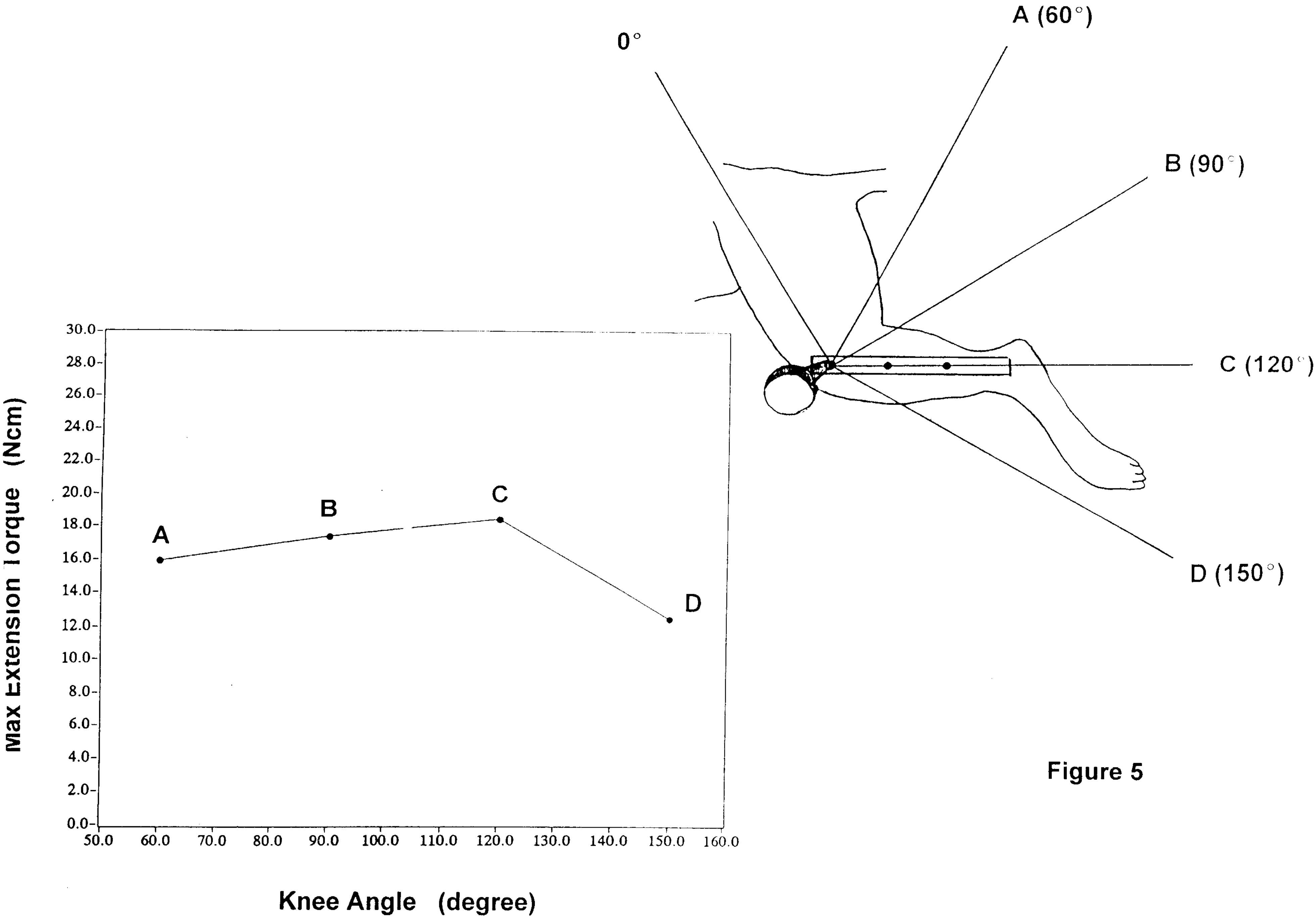

Flexion
EMG Amplitude (mV)
Time (sec)
5.00
4.00
3.00
2.00
1.00
0.00
1.00
2.00
3.00
4.00
5.00
5.00 5.05 5.10 5.15 5.20 5.25 5.30 5.35 5.40 5.45 5.50

Figure 4



0°
A (60°)
B (90°)
C (120°)
D (150°)
A
B
C
D
Max Extension Torque (Ncm)
30.0
28.0
26.0
24.0
22.0
20.0
18.0
16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
Knee Angle (degree)

Figure 5